High SUVmax on FDG-PET Indicates Pleomorphic Subtype in Epithelioid Malignant Pleural Mesothelioma

Supportive Evidence to Reclassify Pleomorphic as Nonepithelioid Histology

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Background: We have recently proposed to reclassify the pleomorphic subtype of epithelioid malignant pleural mesothelioma (MPM) as nonepithelioid (biphasic/sarcomatoid) histology because of its similarly poor prognosis. We sought to investigate whether preoperative maximum standardized uptake value (SUVmax) on ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET) correlates with histologic subtype in MPM.

Methods: Clinical data were collected for 78 patients with MPM who underwent preoperative FDG-PET. We retrospectively classified the epithelioid tumors into five subtypes: trabecular, tubulopapillary, micropapillary, solid, and pleomorphic. Tumors were categorized by SUVmax into two groups: low (<10.0) and high (≥10.0).

Results: The median overall survival of epithelioid tumors with high SUVmax (n = 12) was significantly shorter (7.1 months) than that of epithelioid tumors with low SUVmax (n = 54, 18.9 months, $p < 0.001$) and comparable to nonepithelioid tumors (n = 12, 7.2 months). Epithelioid tumors with pleomorphic subtype (n = 9) had marginally higher SUVmax (mean ± SD: 10.6 ± 5.9) than epithelioid nonpleomorphic subtype (n = 57, 6.5 ± 3.2, p = 0.050), and were comparable to that of nonepithelioid tumors (n = 12, 9.1 ± 4.8). Among the epithelioid tumors with high SUVmax (n = 12), 50% (n = 6) showed pleomorphic subtype. In contrast, among epithelioid tumors with low SUVmax (n = 54), 6% (n = 3) showed epithelioid pleomorphic subtypes (p = 0.001). A positive correlation between mitotic count and SUVmax was observed (r = 0.30, p = 0.010).

Conclusions: Pleomorphic subtype of epithelioid MPM showed higher SUVmax than the epithelioid nonpleomorphic subtype and was similar to nonepithelioid histology. Preoperative SUVmax on FDG-PET in epithelioid MPM can indicate patients with pleomorphic subtype with poor prognosis, supporting their reclassification as nonepithelioid.

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Key Words: Mesothelioma, Pleural neoplasm, Positron emission tomography, Pleomorphic.

Diffuse malignant pleural mesothelioma (MPM) is an uncommon but aggressive tumor with median survival of 9 to 12 months despite multimodal therapy (surgery, chemotherapy, and radiation therapy).[1] Histology and tumor, node, metastases (TNM) stage are the only standard predictors of survival.[2–4] Although epithelioid MPM has a better prognosis than nonepithelioid (biphasic and sarcomatoid) tumors, prognosis within epithelioid histology is variable. We have recently reported the prognostic utility of histologic subtyping in epithelioid MPM, and proposed that the pleomorphic subtype should be reclassified as nonepithelioid histology because of similar clinical outcomes.[5] However, to the best of our knowledge, the biological reasons for this similarity in prognosis remain unexplored.

^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET) is a standard radiographic tool in clinical practice, which assesses the metabolic activity of tumor cells.[6–8] In addition to facilitating prognosis, maximum standardized uptake value (SUVmax) on FDG-PET reflects histology in lung cancer. SUVmax is significantly lower in lung adenocarcinoma than in squamous cell carcinoma.[9–11] To investigate the biology of the pleomorphic subtype in epithelioid MPM, our aim in this study was to determine the correlation between preoperative SUVmax and histologic subtypes of epithelioid MPM. In addition, we investigated the correlation between SUVmax and tumor proliferation on the basis of mitotic count.

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PATIENTS AND METHODS

Patients

Tumor slides were available for 148 patients who received a diagnosis of MPM between 1998 and 2009 at Memorial Sloan-Kettering Cancer Center (MSKCC). Of these, 78 patients underwent FDG-PET before surgical resection. Fifty of 78 patients (64%) underwent PET scans at MSKCC. Seventy-one patients (91%) were not treated with any chemotherapy before the PET scans. Clinical information was collected through a database maintained by the Thoracic Service, Department of Surgery at MSKCC. Institutional review board approval was obtained at MSKCC before the study began. There were 66 patients with epithelioid tumors and 12 with nonepithelioid tumors (six biphasic and six sarcomatoid). Clinical variables recorded in the prospectively maintained database included age, sex, laterality, TNM stage, and surgical procedure. TNM staging was based on the reported imaging findings, the surgeon's intraoperative findings, and the pathologic evaluation of the resected specimens using the 6th edition of the *American Joint Commission on Cancer Staging Manual*.[12] All patients were followed until date of death or last follow-up.

Pathologic diagnosis was based on standard histologic, histochemical, and immunohistochemical criteria.[13–15] As a positive marker of immunohistochemistry for MPM, we used standard immunohistochemical markers including calretinin, WT-1, cytokeratin 5/6, and D2-40. As negative markers for MPM, we used carcinoembryonic antigens, CD15, B72.3, BerEP4, and thyroid transcription factor-1. In addition, pathologic diagnosis was correlated with gross distribution of the tumor and absence of an intrapulmonary lesion on radiologic imaging.

Technique of FDG-PET

The following technique was used for PET scans performed at MSKCC. Patients received 10 to 15 mCi (370–555 MBq) of FDG intravenously. Patients were instructed to fast for 6 hours or more before injection; plasma-glucose levels were measured before imaging. Approximately 60 minutes after injection, torso images were acquired with either GE Advance (GE Medical Systems, Waukesha, WI) or HR plus (Siemens/CTI, Knoxville, TN) PET scanners. Beginning in November 2001, studies were also acquired on hybrid PET/computed tomography (CT) imaging systems, including the Biograph (Siemens/CTI, Nashville, TN) and Discovery LS (GE Medical Systems, Waukesha, WI). The Biograph data was acquired in three-dimensional (3D) mode. All the other scanners used two-dimensional (2D) PET image acquisition. Discovery LS incorporates a PET Advance tomograph, and Biograph incorporates an HR plus PET tomograph. For PET/CT, a low-dose CT scan was acquired first to allow for PET attenuation, correction, and anatomic localization of PET abnormalities. Each PET dataset was reconstructed for image display using iterative algorithms, with and without attenuation correction. Experienced radiologists with specific expertise in nuclear medicine interpreted PET imagery at the time of diagnosis. Uptake of FDG by tumor was quantified by PET region-of-interest analysis with the SUVmax. SUV was calculated as:

$$\text{SUV} = \frac{(\text{Decay-corrected activity[kBq]/tissue volume [ml]})}{(\text{Injected-FDG activity [kBq]/body weight [g]})}$$

Histologic Evaluation

All available hematoxylin and eosin–stained slides (median 7, range, 1–43 slides/case) of epithelioid MPM lesions were reviewed by a single pathologist (K.K.) for the purpose of this study, using an Olympus BX51 microscope (Olympus, Tokyo, Japan) with a standard eyepiece of 22 mm diameter; problem cases were reviewed by two pathologists (W.D.T. and K.K.). Histologic classification for epithelioid MPM was done according to the 2004 World Health Organization criteria (<10% sarcomatoid component).[15] Epithelioid MPM comprised one or more of five histologic patterns,[5] which were recorded in 5% increments: (1) trabecular, (2) tubulopapillary, (3) micropapillary, (4) solid, and (5) pleomorphic. Tumors were classified as pleomorphic subtype when cytologic pleomorphism comprised at least 10% of the tumor.[5] The remaining tumors were classified according to the predominant histologic patterns.

Mitoses were evaluated using high-power-field (HPF) at ×400 magnification (0.237 mm^2 field of view) in the 50 HPF areas with the highest mitotic activities,[16–19] and counted as an average of mitotic figures per 10 HPF. In the cases in which only small areas of viable tumor were available for review, the best attempt was made to assess the equivalent of 10 full HPFs of viable tumor for mitosis counting.[17]

We also recorded the following histological factors: presence of lymphatic or vascular invasion, necrosis (%), fibrosis (%), and myxoid change (%).

Statistical Analysis

Associations between clinicopathologic variables and histologic findings were analyzed using a Fisher's exact test for categorical variables and Wilcoxon test for continuous variables. Overall survival (OS) after surgery was estimated using the Kaplan-Meier method, with patients censored if they were alive at the time of last follow-up. An analysis of time to recurrence (TTR) was restricted to patients who underwent surgery that was deemed to be a complete resection. Nonparametric group comparisons were performed using log-rank test. All p values were based on two-tailed statistical analysis and a p value < 0.05 was considered to indicate statistical significance. All analyses were performed using SAS statistical software (version 9.2; SAS Institute Inc., Cary, NC).

RESULTS

Clinicopathologic Demographics and Their Associations With OS

The clinicopathologic profile of 66 patients with epithelioid MPM is outlined in Table 1. Median age was 63 (range, 29–81); and 65% (n = 43) were men. The tumor involved the left pleura in 50% (n = 33) of the cases. Three patients (5%) were stage I, 16 (24%) were stage II, 33 (50%) were

TABLE 1. SUVmax Associations with Clinicopathologic Factors in Patients With Epithelioid Malignant Pleural Mesothelioma

Variables	N	SUVmax (mean ± SD)	*p* Value
All patients	66	7.1 ± 3.9	
Age			0.454
≤65	26	7.5 ± 4.3	
>65	40	6.3 ± 3.1	
Sex			0.086
Female	23	6.6 ± 4.8	
Male	43	7.3 ± 3.3	
Laterality			0.640
Left	33	7.5 ± 4.5	
Right	33	6.6 ± 3.1	
T stage			0.530
T1	6	6.1 ± 3.8	
T2	24	6.6 ± 3.7	
T3	25	8.1 ± 4.5	
T4	11	6.1 ± 2.6	
N stage			0.240
N0	42	6.8 ± 4.1	
N1	4	7.6 ± 2.5	
N2	20	7.5 ± 3.7	
Stage			0.490
I	3	6.8 ± 5.4	
II	16	6.5 ± 4.1	
III	33	7.6 ± 4.2	
IV	14	6.5 ± 2.4	
Chemotherapy before PET			0.867
Yes	6	7.1 ± 3.5	
No	60	7.1 ± 4.0	
Pleurodesis before PET			0.805
Yes	16	6.8 ± 3.7	
No	50	7.1 ± 4.0	
Lymphatic invasion			0.750
Absence	38	6.9 ± 3.9	
Presence	28	7.2 ± 3.9	
Vascular invasion			0.054
Absence	53	6.6 ± 3.6	
Presence	13	9.1 ± 4.5	
Fibrosis			0.330
<50%	43	7.6 ± 4.4	
≥50%	23	6.1 ± 2.5	
Necrosis			0.042
<10%	59	6.6 ± 3.4	
≥10%	7	10.8 ± 5.8	
Myxoid			0.820
<50%	61	7.0 ± 3.9	
≥50%	5	7.2 ± 3.7	
Histologic subtype			0.050
Nonpleomorphic	57	6.5 ± 3.2	
Pleomorphic	9	10.6 ± 5.9	

SUVmax, maximum standard uptake value; PET, positron emission tomography.

stage III, and 14 (21%) were stage IV. Six patients (9%) were treated with chemotherapy before PET scan. Sixteen patients (24%) underwent pleurodesis before PET scans. Eleven of them (67%) underwent pleurodesis more than 1 month before PET. By surgical procedure, 37 (56%) underwent extrapleural pneumonectomy, 21 (32%) underwent pleurectomy-decortication, and the remaining eight (12%) had other procedures (three biopsies, four exploratory thoracotomies, and one palliative pleurectomy). Lymphatic invasion was detected in 42% ($n = 28$) and vascular invasion in 20% ($n = 13$). By histologic subtype, nine tumors (14%) were pleomorphic and 57 (86%) were nonpleomorphic. In the six patients with epithelioid MPM, who underwent chemotherapy before PET scan, one tumor was pleomorphic and five were nonpleomorphic.

Median OS was 16.3 months. On univariate analyses, necrosis greater than or equal to 10% was associated with shorter OS ($p = 0.002$). No other clinicopathologic factors were significantly associated with OS.

SUVmax and Its Association With OS and TTR

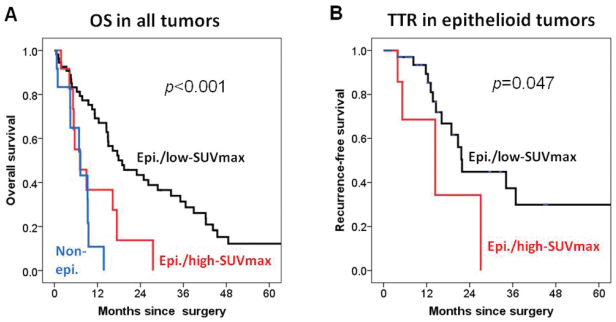
Among the epithelioid MPM lesions, SUVmax ranged from 1.7 to 21.0 (median 6.3, mean ± SD 7.1 ± 3.9). Tumors were classified into two groups by SUVmax as previously reported: low SUVmax less than 10 and high SUVmax greater than or equal to 10.[20,21] The median OS of patients with epithelioid tumors with high SUVmax ($n = 12$) was significantly shorter (7.1 months) than that of patients with epithelioid tumors with low SUVmax ($n = 54$, 18.9 months, $p < 0.001$), and comparable to patients with nonepithelioid tumors ($n = 12$, 7.2 months), as shown in Figure 1*A*.

We have recently proposed to reclassify the pleomorphic subtype of epithelioid MPM as nonepithelioid histology,[5] so we repeated our analysis of SUVmax in a cohort of patients with epithelioid MPM, excluding the nine pleomorphic cases. Among these 57 epithelioid cases, those with epithelioid tumors with high SUVmax ($n = 6$) had a shorter median OS (5.6 months) than those with low SUVmax ($n = 51$, 19.4 months, $p = 0.005$).

Recurrence was observed in 19 of the 44 patients with epithelioid tumors that underwent complete resection; the median TTR for patients with epithelioid tumors with high SUVmax ($n = 7$) was significantly shorter (14.4 months) than for low SUVmax ($n = 37$, 21.9 months, $p = 0.047$), as shown in Figure 1*B*.

Association Between SUVmax and Histology

Within the epithelioid MPM, tumors with pleomorphic subtype ($n = 9$) had the highest SUVmax (mean ± SD: 10.6 ± 5.9), followed by solid ($n = 20$, 6.5 ± 2.9), micropapillary ($n = 10$, 6.1 ± 2.8), tubulopapillary ($n = 18$, 6.7 ± 4.0), and trabecular ($n = 9$, 6.7 ± 3.0) (Fig. 2*A*). Epithelioid tumors with pleomorphic subtype had a marginally higher SUVmax than epithelioid nonpleomorphic subtype ($n = 57$, 6.5 ± 3.2, $p = 0.050$). Nonepithelioid MPM ($n = 12$) seemed to have higher SUVmax (9.1 ± 4.8) compared to epithelioid tumors ($n = 66$, 7.1 ± 3.9), although the difference was not significant ($p = 0.160$).



Histology		n	Median OS
Epithelioid			
	low-SUVmax	54	18.9
	high-SUVmax	12	7.1
Non-epithelioid		12	7.2

SUVmax	n	Median TTR
low-SUVmax	37	21.9
high-SUVmax	7	14.4

FIGURE 1. Overall survival (OS) and time to recurrence (TTR) by maximum standardized uptake value (SUVmax). *A,* The median OS of patients with epithelioid tumors with high SUVmax ($n = 12$) was significantly shorter (7.1 months) than that of patients with epithelioid tumors with low SUVmax ($n = 54$, 18.9 months) and comparable to patients with nonepithelioid tumors ($n = 12$, 7.2 months). *B,* In 44 patients with completely resected epithelioid tumors, the median TTR for those with high SUVmax ($n = 7$) was significantly shorter (14.4 months) than that of patients with low SUVmax ($n = 37$, 21.9 months). SUVmax, maximum standardized uptake value.

However, SUVmax of nonepithelioid MPM was similar to that of epithelioid tumor with pleomorphic subtype and significantly higher than that of epithelioid nonpleomorphic subtypes ($p = 0.046$) (Fig. 2*B*). Among the epithelioid tumors with high SUVmax ($n = 12$), 50% ($n = 6$) showed pleomorphic subtype. In contrast, among epithelioid tumors with low SUVmax ($n = 54$), 6% ($n = 3$) showed pleomorphic subtypes ($p = 0.001$).

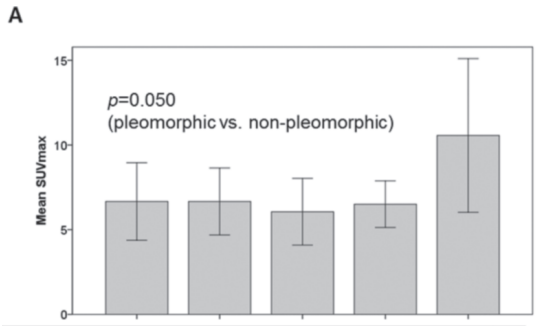
Association Between SUVmax and Clinicopathologic Factors

Associations between SUVmax and clinicopathologic factors in patients with epithelioid MPM are outlined in Table 1. Among these factors, necrosis greater than or equal to 10% was significantly associated with higher SUVmax ($p = 0.042$). When examining mitotic count as a continuous variable, a moderate correlation between mitotic count and SUVmax was observed ($r = 0.30$, $p = 0.010$). Male sex ($p = 0.086$) and vascular invasion ($p = 0.054$) showed a tendency to have higher SUVmax. However, there were no associations among SUVmax and age, disease laterality, TNM stage, chemotherapy before PET scan, pleurodesis before PET scan, lymphatic invasion, fibrosis, or myxoid change (greater than or equal to 50%).

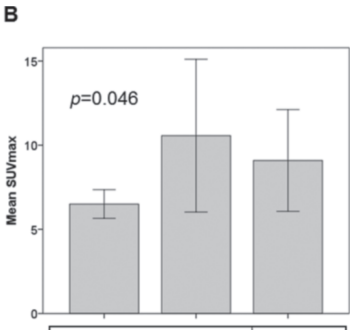
SUVmax of Patients Who Underwent PET Scan at MSKCC and Its Association With OS and Histology

Among the epithelioid MPM patients who underwent PET scan at MSKCC ($n = 43$), SUVmax ranged from 2.3 to 16.5 (median 6.5, mean ± SD: 7.2 ± 3.4). Among the patients who underwent PET scan using Ge-68 transmission rods (GE Medical Systems) without CT ($n = 14$), SUVmax ranged from 3.3 to 15.0 (median 6.6, mean ± SD: 7.2 ± 2.9). Among the patients who underwent PET/CT scan ($n = 29$), SUVmax ranged from 2.3 to 13.4 ($n = 14$, median 4.7, mean ± SD: 5.6 ± 3.0) on Biograph and from 3.6 to 16.5 ($n = 15$, median 8.3, mean ± SD: 8.6 ± 3.6) on Discovery LS.

In the patients who underwent PET scan at MSKCC ($n = 50$), who comprised two third of the total cohort, the median OS of patients with epithelioid tumors with high SUVmax ($n = 7$) was significantly shorter (8.9 months) than that of patients with epithelioid tumors with low SUVmax ($n = 36$, 19.4 months, $p < 0.001$), and comparable to patients with nonepithelioid tumors ($n = 7$, 6.9 months). SUVmax of tumors with epithelioid nonpleomorphic subtypes ($n = 37$, mean ± SD: 6.9 ± 2.9) was lower than that of epithelioid tumors with pleomorphic subtype ($n = 6$, 8.8 ± 5.5) and of nonepithelioid tumors ($n = 7$, 10.1 ± 5.4), although the small sample size did not allow for statistical analysis. Among the epithelioid tumors with high SUVmax ($n = 7$), 43% ($n = 3$) showed pleomorphic subtype. In contrast, among epithelioid tumors with low SUVmax ($n = 36$), 8% ($n = 3$) showed pleomorphic subtypes.



Subtype	Epithelioid histology				
	Trabecular	Tubulopapillary	Micropapillary	Solid	Pleomorphic
n	9	18	10	20	9
SUVmax (mean±SD)	6.7±3.0	6.7±4.0	6.1±2.8	6.5±2.9	10.6±5.9



Epithelioid histology		Non-epithelioid histology
Non-pleomorphic	Pleomorphic	
57	9	12
6.5±3.2	10.6±5.9	9.1±4.8

FIGURE 2. Association between maximum standardized uptake value (SUVmax) and histology. *A,* Within the epithelioid tumors, pleomorphic subtype ($n = 9$) had the highest SUVmax (mean ± SD: 10.6 ± 5.9), followed by solid ($n = 20$, 6.5 ± 2.9), micropapillary ($n = 10$, 6.1 ± 2.8), tubulopapillary ($n = 18$, 6.7 ± 4.0), and trabecular ($n = 9$, 6.7 ± 3.0). *B,* SUVmax of nonepithelioid tumors ($n = 12$, 9.1 ± 4.8) was similar to that of pleomorphic subtype and significantly higher than that of epithelioid nonpleomorphic subtype ($n = 57$, 6.5 ± 3.2). SUVmax, maximum standardized uptake value.

DISCUSSION

Current preoperative therapeutic decisions of MPM are based on histologic type and the TNM stage. To account for the histological heterogeneity among epithelioid MPM, we have recently assessed the prognostic significance of five histologic subtypes, and observed that the pleomorphic subtype resembles the clinical outcome of nonepithelioid (biphasic and sarcomatoid) histology more closely.[5] To gain further insight into the biology of the pleomorphic subtype, we investigated whether the SUVmax reflects the histologic subtypes in epithelioid MPM. On the basis of mitotic count in patients with epithelioid MPM, we demonstrated that high SUVmax was associated not only with disease recurrence and OS, but also with increased proportion of pleomorphic subtype and proliferative activity.

Pleomorphic subtype is defined as having more than10% of the tumor demonstrating pleomorphism.[5] Accurately identifying these patients before deciding on appropriate therapeutic management is difficult because the small proportion of pleomorphism may not be obvious on small diagnostic biopsy samples. Yet, given their poor prognosis (median OS = 8.1 months),[5] the ability to recognize this population is critical to clinical decision-making. In the current study, we observed that the nine epithelioid tumors with pleomorphic subtype were characterized by having higher SUVmax (mean SUVmax = 10.6) compared to epithelioid nonpleomorphic subtypes (mean SUVmax = 6.1–6.7) (Fig. 2*A*). Among the patients with epithelioid MPM with SUVmax greater than 10, half had the pleomorphic subtype, whereas for those with SUVmax less than 10, the majority (94%) had the nonpleomorphic subtype. Though it is difficult to precisely correlate the pleomorphic area on microscopic examination to the site of SUVmax on FDG-PET, the association we observed may help in preoperative identification of the pleomorphic subtype.

Furthermore, we observed a similarity in the SUVmax of the pleomorphic subtype (mean SUVmax = 10.6) and the nonepithelioid histology (mean SUVmax = 9.1) (Fig. 2*B*). In our previous report we demonstrated the resemblance in outcomes between the pleomorphic subtype and the nonepithelioid histology (the pleomorphic subtype experienced median OS of 8.1 months compared to 7.0 months and 3.0 months for biphasic and sarcomatoid, respectively).[5] Our current observation provides radiographic evidence that the pleomorphic subtype resembles the nonepithelioid MPM more closely than the epithelioid histology, and further strengthens our proposal to reclassify the pleomorphic subtype under the nonepithelioid histology.

High FDG uptake has been shown to correlate with decreased survival in patients with MPM.[20–23] However, these studies were heterogeneous in morphology because they included nonepithelioid tumors. Therefore, the prognostic utility of FDG uptake was unclear in a uniform cohort that comprised epithelioid histology. Within our cohort of 66 patients with epithelioid MPM, a cutoff of SUVmax 10 significantly stratified OS, and this finding remained significant even after excluding patients with pleomorphic subtype.

In our study, 24% of epithelioid MPM patients underwent pleurodesis before PET scans. Although the prolonged, marked hypermetabolic pleural activity associated with pleurodesis may potentially limit PET-scan evaluation, the pleural SUVmax in the epithelioid MPM patients who underwent pleurodesis before PET scan showed no significant difference from that of the patients with no prior pleurodesis.

One limitation of the current study is that the PET scans were performed at multiple locations. Because of the rarity of MPM, it is difficult to obtain a large number of scans at a single location. Nevertheless, two thirds of the scans in this study were performed at the same location. To validate our findings with a more uniform group of patients, we performed the subsequent analysis on the patients who underwent PET scan at MSKCC. In this group, the SUVmax remained significant in stratifying OS, and the epithelioid tumor with pleomorphic subtype demonstrated a higher SUVmax than in epithelioid nonpleomorphic subtypes.

One more limitation of our study is that the PET scans were performed by four different scanners at MSKCC, and the SUV differences were observed by the different scanners, attenuation corrections, and acquisition models. Although the use of four different scanners is a potential limitation of this study, our correlations are significant despite the limitations of our study—differences in CT versus rod-source attenuation correction,[24] and differences in acquisition of data in 2D or 3D models.[25] On a more positive note, however, the fact that we were able to detect statistically significant associations between SUVmax versus OS and histology, despite using different scanners, may suggest that (1) our results are generalizable to other medical centers using different scanners than ours and (2) the true correlation between SUVmax versus OS and histology may be underestimated by our results, presuming that using different scanners will weaken such correlation rather than strengthen it. The previous report suggested the SUV differences by the different acquisition models (2D or 3D).[25] In our study, the Biograph data were acquired in 3D mode, and all the other scanners used 2D PET image acquisition. Again, although these technical differences may weaken the ability to detect the correlations that we reported in this study, we detected the correlations despite these technical limitations, not because of them.

Although future studies should normalize SUVmax by different scanners, our findings confirm its prognostic value. In a recent report, Nowak et al.[26] proposed a prognostic model that incorporates total glycolytic volume (TGV) on FDG-PET to account for the tumor volume in addition to the metabolic activity. Interestingly, in their cohort of 89 patients, TGV was prognostic whereas SUVmax was not. We did not record TGV in the current study.

In addition to prognosis, SUVmax correlates with a higher proliferation index in lung cancer.[7,27] However, the correlation between SUVmax and proliferative factors, such as Ki-67 labeling index and mitotic count, has not been investigated in MPM. In our study, higher SUVmax showed a correlation with higher mitotic count, demonstrating that FDG uptake by MPM tumor cells reflects proliferative activity. We also demonstrated that necrosis correlates with higher SUVmax. These findings confirm that SUVmax reflects tumor biology in addition to having prognostic value.

In conclusion, we have demonstrated in this study a radiologic–pathologic correlation in epithelioid MPM through comparison using a noninvasive imaging modality that measures tumor metabolism (SUVmax on FDG-PET) and histologic characterization on microscopic examination (histologic subtype). We observed that (1) high SUVmax correlates with pleomorphic subtype in epithelioid MPM, thus providing radiologic resemblance of the pleomorphic subtype with the nonepithelioid tumors, and (2) epithelioid MPM with high SUVmax should be considered as having a poorer prognosis, similar to nonepithelioid tumors. As this is a retrospective study, these findings should be validated prospectively. Nonetheless, our findings emphasize the importance of a multidisciplinary approach in both predicting patient outcomes and better understanding of a heterogeneous disease such as MPM.

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